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6. (Amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a fragment thereof of a botulinum toxin type A or biologically active variants thereof.

13. (Amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin, a butyricum toxin, a tetani toxin or biologically active variants thereof.

BA

14. (Amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin type A, B, C1, D, E, F, G or biologically active variants thereof.

15. (Amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin type A or biologically active variants thereof.

16. (Amended) An agent according to claim 15 wherein the fragment of the heavy chain comprises at least a portion of the amino terminal fragment of the heavy chain.

Remarks

This is in response to the Examiner's communication mailed November 25, 2002. A response is due February 25, 2003. Accordingly, this response is being timely filed.

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Claims 1-21, 23-28, 30-44, and 68-71 were pending. By way of this response, claims 4-6 and 13-16 have been amended. Support for the amendments to the claims can be found in the application as filed, and no new matter has been added. Accordingly, claims 1-21, 23-28, 30-44, and 68-71 remain pending.

Applicant acknowledges that the response filed October 10, 2002 was sufficient to overcome the previous rejections under 35 U.S.C. § 112, first paragraph, and 35 U.S.C. §§ 102 and 103. Claims 1-16, 25-27, 30-40, 42-44, 68 and 69 have now been rejected under 35 U.S.C. § 112, second paragraph, and/or 35 U.S.C. § 102(a). Applicant addresses those rejections herein.

Item 2 of the Office Action-Rejections Under 35 U.S.C. § 112, second paragraph

Claims 4-6, and 13-16 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In particular, the Office Action states that claims 4-6 and 13-15 are indefinite because of the recitation of the phrase "variants thereof", and that the phrase "the fragment" in claim 16 does not have proper antecedence in claim 1.

Applicant has amended claims 4-6 and 13-16 as set forth above, and respectfully traverses the rejections as they relate to the amended claims.

Amended claims 4-6 and 13-15 recite "biologically active variants thereof". In other words, the variants of the toxins

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have a biological activity similar to the toxins recited in the claims to obtain a similar therapeutic effect provided by the toxins. Thus, applicant submits that the metes and bounds of the phrase "variants thereof" are now clearly defined, and the claims are not indefinite. In addition, claims 4 and 13 have been amended to correct the spelling of botulinum toxin.

Regarding claim 16, applicant has amended claim 16 to be dependent from claim 15, which provides proper antecedence for "the fragment" of claim 16.

Further, applicant submits that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims be withdrawn.

Items 3-4 of the Office Action-Rejections Under 35 U.S.C. § 102

Claims 1-3, 7-12, 25-27, 30-34, 36-40, 42-44, 68, and 69 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated by, Sawamura et al. (Journal of Neuroscience, December 15, 2000). Applicant traverses this rejection.

As indicated above, the claims have only been amended to address the § 112 rejections, and have not been amended to overcome the prior art. In addition, applicant does not concede that Sawamura et al. is prior art to the claimed invention, and applicant reserves the right to antedate Sawamura et al. in the future, if desired.

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As indicated in applicant's previous response, a claim is anticipated only if each and every element recited in the claim is disclosed in a single prior art reference. Applicant respectfully traverses the rejections under 35 U.S.C. § 102, and submits that Sawamura et al. does not anticipate the claimed invention because Sawamura et al. fails to expressly or inherently teach each and every element recited in the claims.

Sawamura discloses the use of a conjugate of saporin and an antibody to dopamine β hydroxylase (p. 9243, left column, second full paragraph). Neither the saporin nor the antibody to dopamine β hydroxylase is a targeting ligand that binds to the alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s), as recited in the pending claims. Saporin is a toxin that inactivates ribosomes and inhibits protein synthesis. An antibody to dopamine β hydroxylase is an antibody that binds to dopamine β hydroxylase. The Office Action fails to provide any evidence, or indicate where Sawamura et al. disclose, that saporin or the antibody to dopamine β hydroxylase binds to alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s). The remarks made by the Examiner do not support the Examiner's position that Sawamura et al. discloses a ligand that binds alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s). In contrast, Sawamura et al. specifically teach that the saporin acts on the ribosomes, and the antibody to dopamine β hydroxylase binds to dopamine β hydroxylase. Accordingly, Sawamura et al. does not anticipate the claims. To the extent the Examiner maintains the rejection, applicant requests the Examiner to specifically indicate where Sawamura et al. teaches the ligands recited in the claims.

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In addition, Sawamura et al. fails to provide any suggestion or motivation to use a ligand for alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s) conjugated to a therapeutic component, and thus, Sawamura et al. does not render the claimed invention obvious.

In view of the above, applicant submits that the present claims 1-3, 7-12, 25-27, 30-34, 36-40, 42-44, 68, and 69 are not anticipated by, and are unobvious from and patentable over, Sawamura et al. under 35 U.S.C. §§ 102(a) and 103(a).

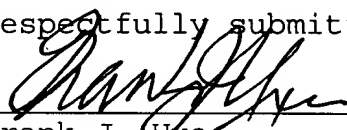
In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present agents and methods for making the agents including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

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In conclusion, applicant has shown that the present claims satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1-21, 23-28, 30-44, and 68-71 are allowable. Applicant requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

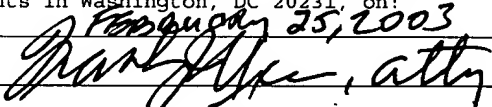
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Respectfully submitted,


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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal service as first class mail in an envelope addressed to: Commissioner for Patents in Washington, DC 20231, on:

February 25, 2003

2/25/03

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 4-6 and 13-16 have been amended as follows:

4. (Amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a fragment thereof of a [botulimum] botulinum toxin, a butyricum toxin, a tetani toxin or biologically active variants thereof.

5. (Amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a fragment thereof of a botulinum toxin type A, B, C1, D, E, F, G or biologically active variants thereof.

6. (Amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a fragment thereof of a botulinum toxin type A or biologically active variants thereof.

13. (Amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a [botulimum] botulinum toxin, a butyricum toxin, a tetani toxin or biologically active variants thereof.

14. (Amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin type A, B, C1, D, E, F, G or biologically active variants thereof.

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15. (Amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin type A or biologically active variants thereof.

16. (Amended) An agent according to claim [12] 15 wherein the fragment of the heavy chain comprises at least a portion of the amino terminal fragment of the heavy chain.